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EXAMINER	
FOLEY, SHANON A	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	08/591,651	CLASSEN, JOHN B.	
	Examiner	Art Unit	
	SHANON A. FOLEY	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/27/2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *78-83 and 85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5, 6, 8, 10, 11, 16, 27-30, 32-41, 43, 44, 46, 49-52, 55-57, 59-68, 71-74, 77, 84, 86-88, 90-112, 115-128, 144-152, 259 and 266-303* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/05/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 5,6,8,10,11,16,27-30,32-41,43,44,46,49-52,55-57,59-68,71-74,77-88,90-112,115-128,144-152,259 and 266-303.

DETAILED ACTION

The Group and/or Art Unit of your application has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1619, Examiner Foley.

Prosecution is being reopened in this case. The record in this application reveals that Applicant received a Final rejection on November 5, 2001. This is followed by a Notice of Appeal on May 6, 2002, two amendments, submitted May 6, 2002 and June 21, 2002, and two Advisory Actions, mailed June 4, 2002 and August 20, 2002, in response to the two amendments. These papers are followed by 20 Declarations filed on October 18, 2002 and an Appeal Brief filed November 6, 2002. An Advisory Action mailed November 18, 2002 indicates that the Declarations are not compliant with 37 CFR § 1.116. In response, Applicant filed a Petition to have the Declarations entered. This Petition was denied by the Office on February 6, 2003. Also mailed was a Notification of Non-Compliance under 37 CFR § 1.192(c), regarding the defective Appeal Brief filed November 6, 2002. This is followed by a second Petition to reconsider the Petition Decision mailed February 6, 2003. This second Petition was also denied by the Office on July 16, 2003. A second Appeal Brief was received August 8, 2003. In response, the Office re-opened prosecution with a restriction requirement mailed June 18, 2004, since a review of the record indicated that this application was still not ripe for appeal in view of the large number of inventions and/or species that were not restricted one from another. As such, both the Office and Applicant missed numerous formality problems in the claims as well as substantive enablement issues. Although Applicant responded to this restriction requirement, a

second restriction requirement was also issued by the Office on December 12, 2006. However, this last restriction requirement is vacated for reasons explained below.

Election/Restrictions

In the response received March 27, 2007 to the restriction requirement mailed December 12, 2006, applicant's election of a species of claim 276 as "at least nonavalent" has been received. The election is made with traversal on the grounds that the species are overlapping since "at least octavalent", recited in claim 275, includes nonavalent agents.

Applicant's traversal has been fully considered, but is found unpersuasive since claim 275 clearly falls within the scope of the elected species. There is no traversal presented for how mono-, di-, tri-, tetra-, penta-, hexa- or hepta- valent immunogenic agents are obvious variants to the elected "at least nonavalent". Since no argument to the effect is presented, it is determined that the election is made without traverse. However, since it is determined that examination of all species would not be burdensome, the species requirement is withdrawn.

It is noted that the restriction mailed December 12, 2006 also required an election of one type of immunogenic agent to be elected for claims 268-276 and 284-291, see page 2. It is also noted that Applicant failed to respond to this portion of the restriction requirement. However, upon review of the election received July, 28, 2004, in response to the restriction requirement mailed June 18, 2004, it is clear that applicant elected Group I, drawn to a kit, immunogenic compositions (since these should have been included with the claims of Group I, as discussed in the interview of July 27, 2004) and methods of reducing the severity or incidence of an immune disorder. Applicant further elected species (B), drawn to bacterial immunogen, species (L), drawn to meningitis caused by meningococci, as well as species (1), drawn to diabetes.

Therefore, the requirement of a species election of one type of immunogenic agent to be elected in the restriction of December 12, 2006 is erroneous since the election was already previously indicated by applicant.

Regarding the species elections in the response received July 28, 2004, applicant elected Group I with traverse. The traversal is on the grounds that previous examination encompassed immunogenic agents and kits, and that these should remain examined together. The examiner agrees. Therefore, claims drawn to immunogenic agents and kits will be examined together. Applicant also elected the bacterial immunogen "with traverse", but this phrase is not supported by arguments or reasoning to support the traversal. Regarding the election of meningitis and diabetes, applicant submits no arguments or traversal with respect to these species elections. Therefore, it is determined that the species elections made for meningitis and diabetes is made without traverse. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Accordingly, claims 78-83 and 85 are withdrawn from consideration.

In summary, claims 5, 6, 8, 10, 11, 16, 27-30, 32-41, 43, 44, 46, 49-52, 55-57, 59-68, 71-74, 77-88, 90-112, 115-128, 144-152, 259 and 266-303 are pending. Claims 78-83 and 85 are withdrawn from consideration due to non-elected subject matter. Claims are 5, 6, 8, 10, 11, 16, 27-30, 32-41, 43, 44, 46, 49-52, 55-57, 59-68, 71-74, 77, 84, 86-88, 90-112, 115-128, 144-152, 259 and 266-303 under consideration.

Response to Formal Matters

In the response to the restriction requirement received July 28, 2004, Applicant states that (1) the Declaration of October 18, 2002 with its 19 exhibits and (2) the IDS submitted December 12, 2002, should be entered as a matter of right since prosecution is being reopened.

Applicant's reasoning has been considered, but is found deficient since the papers of (1) and (2) were denied entry twice in a petition decisions mailed February 6, 2003 and again on July 16, 2003. For the reasons enumerated in the Petition Decisions, (1) and (2) will not be entered for reasons of record.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on October 5, 2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Objections

There are numerous informalities. Although it is believed that all of the informalities are mentioned herein, Applicant is encouraged to proof-read the claims before re-submission. The following claims are objected to because of the following informalities: Recitation of a genus or a genus/species should be italicized. *Hemophilus influenza* in claims 37, 55, 71, 121, 123, 124 and 148 should be italicized. Similarly, recitation of "Neisseria" in claims 37 144, 149 and 150 should also be italicized. "[A]cting" in line 2 of claim 36 should syntactically be "acts". "BCG" is listed twice in claim 37. Claims 73 and 88 have erroneous periods in lines 3 and 2, respectively. It appears that claim 128 is missing "developing" between "of" and "a" in line 2. Claim 281 is missing a period. Claim 259 is missing "the" between "of" and "first" in line 6.

Claim 259 is also missing "is" in line 7 before "protective" and the phrase, "at least of said" bridging lines 7-8 of claim 259 is syntactically incorrect. In line 14 of claim 267 and line 4 of claim 303 "on" should be "one". Claim 295 states that an immunogen conjugated to a different carrier "was" associated with a decreased risk, see line 5. If any remaining informality exists in the claims and is inadvertently not discussed here, appropriate correction is required by Applicant.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 6, 8, 10, 11, 16, 27-30, 32-41, 43, 44, 46, 49-52, 55-57, 59-68, 71-74, 77, 84, 86-88, 90-112, 115-128, 144-152, 259 and 266-303 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is unclear for a couple of reasons. The claim recites the limitation "one such immunogen" in line 2. This claim depends from claim 32, where "one or more immunogens" in lines 3-4 are administered. It cannot be determined which of the immunogens administered in claim 32 could be referenced specifically by "one such immunogen" since the "one such immunogen" is administered in claim 6 at a "substantially greater" dosage than is required for immunization against the infectious disease with which it is associated. Since any one of the "one or more immunogens" recited in claim 32 could be "one such immunogen", it cannot be determined which "one such immunogen" is required to be administered at a "substantially greater" dosage in claim 6. Which immunogen in claim 32 is administered differently in claim

6? In addition, it is indeterminable what would be a requisite degree of "substantially greater" when no point of reference is provided in the claims or the disclosure.

The meaning of claims 8, 10, 11, 16, 32, 34, 35, 38-41, 49-52, 59-65, 86, 96, 97, 100, 102, 109 and 118-120 is unclear since these claims are not methods and there are no active method steps recited. These claims depend from the kit of claims 27 and 59. Claim 27 recites intended use for the kit in the "instructions", while claim 59 recites "information" in subsections (a), (b) and (c) of the claim. "[F]ollowing such instructions" or "labeling indications", recited in the claims does not impart patentable distinctness on the components in the kit since printed matter is not functional, see MPEP § 2112.01 and *In re Gulack*, 703 F.2d 1381, 1385-86, 217 USPQ 401, 404 (Fed. Cir. 1983) ("Where the printed matter is not functionally related to the substrate, the printed matter will not distinguish the invention from the prior art in terms of patentability .... [T]he critical question is whether there exists any new and unobvious functional relationship between the printed matter and the substrate."). Since there is no functional relationship between the components in the kit and the paper the instructions are provided on, the printed material is indistinguishable between the claims. While the physical actions of "following such instructions" differ, there are no physical steps accomplished since the limitations of the kit comprise mere paper and immunogens in containers. There are no method steps and the claims are not drawn to a method. Therefore, the full meaning of the claims is unclear. For the purpose of comprehensive examination, claims depending upon "instructions" of any sort will be interpreted as actual components, if actual components are recited.

Claims 66-68, 72-74, 117, 126, 150, 266, 267, 278, 279, 295, 298 and 299 recite "pediatric" and "non-pediatric" immunogens. It is noted that a similar rejection was withdrawn

on page 8 of the Final rejection mailed May 4, 1999 due to the list of immunogens recited in the disclosure. On page 35 of the instant disclosure, it is noted that the term "pediatric immunogen" refers to immunogenic inoculates administered to children less than 16 weeks old. A list of immunogens follows, but the disclosure specifically states that the list is non-limiting. In the paragraph bridging pages 35-36, "non-pediatric" immunogens are defined as immunogenic inoculates administered to children older than 112 days. Since the lists provided for each group are not exhaustive and each group of immunogens/diseases are so varied in etiology, histology, pathogenesis, symptomology and histology, it is determined that the skilled artisan would be unable to distinguish what is intended by "non-pediatric immunogens" and "pediatric immunogens", especially since even scheduled inoculations are not administered in a synchronized fashion to every child and since the two groups of children less than 16 weeks old and older than 112 days are still under pediatric care. While applicant may be his own lexicographer, claim terms are to be given their ordinary and customary meaning by clearly setting forth a definition of the term that is different from its ordinary and customary meaning(s). *See In re Paulsen*, 30 F.3d 1475, 1480, 31 USPQ2d 1671, 1674 (Fed. Cir. 1994). Since the meaning of "pediatric immunogens" and "non-pediatric immunogens" is not clearly defined within the disclosure, the terms are rendered vague and indefinite. This rejection also affects dependent claims.

Claim 33 recites the limitation "immune-mediated disorder" in line 9. While the claim refers to "an immune disorder" in line 2, there is a distinct difference between a disorder mediated by the immune system and a broader genus of immune disorders. Therefore, there is insufficient antecedent basis for this limitation in the claim.

Claim 36 states that one of the immunogens "also act[s]" to reduce the incidence of infectious disease. Since immunogens are not art-recognized to have any sort of behavior, it cannot be determined what is intended by "acting". In the interest of comprehensive prosecution, the meaning of the claim will be interpreted to mean that presentation of the immunogen to the immune system reduces the incidence of a corresponding infectious disease.

Claim 87 recites the limitation "said immunosuppressant" in line 2. There is insufficient antecedent basis for this limitation in the claim. This claim depends from claim 59, which does not refer to an immunosuppressant. Therefore, it is suggested that "said" in claim 87 be replaced with "an".

Claims 27, 32, 33, 36, 56, 103 and 144-148 state that administering at least one or more immunogens induces an immune response that "substantially reduces" the incidence or severity of at least one chronic immune-mediated disorder. The magnitude intended by any substantial reduction is indeterminate since the specification lacks a standard for measuring the degree intended. Therefore, the claims are unclear. *Ex parte Oetiker*, 23 USPQ2d 1641 (Bd. Pat. App. & Inter. 1992). This rejection also affects dependent claims.

Claim 128 specifically states that immunogens administered "substantially protect" against at least one infectious disease. Again, the requisite degree that would be considered "substantial" cannot be determined since there is no discussion in the instant specification for what is intended by "substantial protection". Claim 128 is also an incomplete method. The method is drawn to reducing the risk of a chronic immune-mediated disorder that is associated with immnization by (1) a determination step and (2) providing the kit of claim 59. There are no

active steps of administration or any active steps recited in the claim that would reduce the risk of a chronic immune-mediated disorder.

Claims 268-276 refer to valency of an immunogenic agent. (It is noted that Applicant did not claim pentavalent). Then specification does not offer a definition for "valent" or "valency". According to Stedman's Medical Dictionary, valent means having valence, see below:

Stedman's Medical Dictionary 27th Edition

valent (va'lent)
Possessing valence

and "valence" is defined as:

valence, valency (va'lens, -len-se)
The combining power of one atom of an element (or a radical), that of the hydrogen atom being the unit of comparison, determined by the number of electrons in the outer shell of the atom (v. electrons); e.g., in HCl, chlorine is monovalent; in H_2O, oxygen is bivalent; in NH_3, nitrogen is trivalent. [L. *valentia,*1 strength]
negative ***v.*** the number of *v.* electrons an atom can take up.
positive ***v.*** the number of *v.* electrons an atom can give up.

Since neither "valent" or "valency" are art-recognized terms for describing a characteristic of an immunogen in terms of valency and there is no definition provided in the instant disclosure for the meaning of the term, no clear meaning can be discerned for these claims.

Claim 280 refers to a "unique" immunological marker. It cannot be determined what kind of characteristic would render a marker "unique".

Claim 281 recites that the "associations [of the immunogen and the carrier protein] are "statistically significant". A requisite comparison teaching to determine whether a degree of association is significant through statistical analysis is not discussed in the instant disclosure. Therefore, the meaning of this claim cannot be determined.

Claims 297-303 state that at least one immunogen is associated with an "acceptable risk" of development of one or more chronic immune-mediated disorders. It is not clear what would be considered an "acceptable risk" or from what perspective this acceptance would be viewed from, the subject administered the immunogens or the physician administering the immunogens.

Claims 300 and 301 are rejected for lack of clarity and indefiniteness for reciting that the agents are "substantially free" of immunomodulators and aluminum salts, respectively. The requisite degree for the presence or absence of either component to be considered "substantially free" in the agent is cannot be discerned because it is not apparent in any discussions within the instant disclosure.

Claim 302 is incomplete. The claim states that the immunogens are associated with an acceptable risk. Risk of what?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5, 84, 87, 88, 106, 116, 127, 144 and 267-303 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

For the sake of comprehensive examination and succinctness, the following is a list of limitations that cannot be found in the instant disclosure or the original claims. There is also no

explanation from Applicant that points to where the following limitations are supported, either implicitly, or explicitly.

1) Claim 5 now recites "*Streptoccocus*" as being excluded from immunogens provided in the kit. Original claim 5 did not list this bacterium and support for its exclusion cannot be located in the instant disclosure. Additionally, original claim 5 recited "*Pneumoccocus*", not pneumoniae, as it does now. Since pneumonia can be caused by antagonists other than *Pneumococcus*, the recitation of pneumoniae constitutes new matter.

2) Claim 87 states that the kit of claim 59 comprises an immunosuppressant. Claim 88 further limits the immunosuppressant to glucocorticoid or any "substance which induces the release of a glucocorticoid hormone". Support for these limitations cannot be found in the instant disclosure or the original claims.

3) Claim 106 states that the at least one immunogen in the method of claim 103 is one "other than smallpox". The exclusion of this disease or immunogen cannot be located implicitly or explicitly in the original application filed.

4) Claim 116 states that the kit of claim 16 provides at least one immunogen that protects at against at least two infectious diseases. There is no support for any one immunogen that protects against at least two different infectious diseases. This embodiment is new matter introduced into the claims. This rejection also affects dependent claims 84 and 127.

5) Claim 144 specifically states that *Streptococcus pneumoniae* is to be specifically excluded from the immunogens administered in the method. There is no clear implicit or explicit support for this limitation in the original claims or the instant disclosure.

6) Claims 267 and 277-279 and 284-291, 294, 295 and 298 refer to (a) carbohydrate immunogens and (b) their conjugation to carrier proteins. While the disclosure briefly mentions that biological immunogens can be carbohydrates on page 35, lines 17-19, there is no explicit or implicit support in the disclosure or the original claims for carbohydrate immunogens or specific meningococcal and pneumococcal carbohydrate immunogens recited in the claims. With regard to conjugation, the only disclosure that can be located is on page 73, lines 25 and 26, but conjugation, or lack of conjugation, is specifically referring to *Hemophilus influenza*. There is no mention in the disclosure what the *Hemophilus influenza* immunogen is conjugated to. There is also no disclosure that implicitly or explicitly teaches conjugating any immunogen and there is no mention of carrier proteins, which constitutes new matter. All dependent claims are also affected.

7) The valencies recited in claims 268-276 is not supported implicitly or explicitly in the original claims or the instant disclosure.

8) Claim 280 refers to a "unique immunological marker". There is no support in the disclosure for these limitations.

9) Claim 281 recites that the "associations [of the immunogen and the carrier protein] are "statistically significant". Neither the associations or the "statistically significant" attributes are mentioned or implied in the instant disclosure.

Applicant is required to either point out where support can be found for these limitations, or cancel the new matter.

Claim 88 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described

in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 88 recites "a substance which induces the release of a glucocorticoid hormone." USPgPub 20070036740 A1, teaches Trabecular meshwork inducement of a glucocorticoid protein, Myoc, see paragraph [0063]. Anderson of US 3, 856,955, teaches stimulation of glucocorticoid using dexamethasone-21-isonicotinate, triamcinolone acetonide, and flumethasone (6.alpha., 9.alpha., difluoro-16.alpha.-methylprednisolone) where the vehicle was an isotonic aqueous suspension and the mode of administration intramuscular injection, see column 6, lines 58-67 and claim 3. Finally, Lipsky of US 5,846,742, discloses and claims an assay that identifies any substance that induces glucocorticoid gene expression using T2 (*Tripterygium wilfordii* Hook F extract) as a control, see column 3, lines 49-57 and column 7, lines 29-52. The components that induce glucocorticoid production are extremely varied and diverse. There is no common elemental structural feature in the art that would identify itself as a glucocorticoid induction agent to one skilled in the art. Due to the lack of discussion, guidance or teaching in the instant disclosure identifying the relevant features of any substance that would induce glucocorticoid, it is apparent that the instant disclosure lacks adequate support for possession of the genus of substances claimed.

Lack of Enablement

Note: the only claim excluded from this rejection is claim 266, since it is only drawn to a pharmaceutical composition comprising immunogenic agents intended to protect against at least one infectious disease.

Claims 5, 6, 8, 10, 11, 16, 27-30, 32-41, 43, 44, 46, 49-52, 55-57, 59-68, 71-74, 77, 84, 86-88, 90-112, 115-128, 144-152, 259 and 267-303 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to kits comprising containers with immunogens. The intended use of these kits and the methods claimed is to administer the immunogens to prophylactically and therapeutically reduce, or "significantly reduce" the incidence or severity of any chronic immune-mediated disorder. Contrary to "prophylactic and therapeutic" intent of previously presented claims, new claims 297-303 state that administration of the immunogens for infectious disease protection is "associated with an acceptable risk" for developing one or more chronic immune-mediated disorders. It is unclear what a requisite degree of "acceptable" would be, or whose point of view is recited in the claims. The majority of claims specify that the immunogens are administered to mammals within the first few months after birth, or are administered to mammals and humans less than 28 days old. Among the immunogens listed in the claims are those described as "pediatric" and "non-pediatric" immunogens. However, these are not art-recognized terms for immunogens or pediatric inoculates and the disclosure fails to provide a definition for what is intended by these descriptors. Within the broad genus of possible immunogens and disorders encompassed by the claims is the elected species of meningococcal immunogens and non-streptozotocin-induced diabetes. Therefore, within the scope of the broad subject claimed and considered under examination is a narrower scope of an

intended use of the instant kits and methods to administer meningococcal immunogens to reduce the incidence or severity of non-streptozotocin-induced diabetes.

The method of claim 128 is particularly perplexing. It's drawn to a method of reducing the risk of a chronic immune-mediated disorder associated with immunization to protect against an infectious disease by:

(1) determining the occurrence of a chronic immune-mediated disorder after immunogen administration or determining the effect of immunizing regiments on the development of a chronic immune-mediated disease, and

(2) providing a kit comprising immunogens and paper instructions.

There are no physically active method steps in this claim that would provide a nexus to the goal of "reducing the risk of a chronic immune-mediated disorder" stated in the preamble. The step of determination is a mental process and the presentment of a kit does not constitute active steps. One skilled in the art would be unable to accomplish any method other than receiving a kit from steps (1) and (2) recited, much less inducing an immune response.

One of ordinary skill in the art would not predict that delivering any immunogen, to a mammal or a human a few months old from birth, selected from (see claim 150 for example):

"an immunogen of an organism which causes measles, mumps, rubella, diphtheria, pertussis, anthrax, plague, encephalitis, meningitis, typhus, typhoid fever, Lyme disease, cholera, leprosy, influenza, varicella, rabies, dengue, toxoplasmosis, coccidiomycosis, schistosomiasis, and malaria, or an immunogen selected from BCG, *hemophilus influenza*, hepatitis B, polio virus, *Streptococcus, staphylococcus, Neisseria*, *Escherichia coli*, *Shigella*, *Leishmania*, cytomegalovirus, respiratory syncytial virus, Epstein-Barr virus, herpes virus, parainfluenza virus, rotavirus, adenovirus, human immunodeficiency virus, hepatitis A virus, and NonA and NonB hepatitis virus immunogens and an immunogen which causes a disease selected from tetanus and polio"

would reduce the incidence or severity of any chronic immune-mediated disorder, much less the elected disorder of non-diabetes. There is no known immune response that would inhibit the incidence or decrease the severity of diabetes or any chronic immune-mediated disease. According to the art cited below, diabetic patients are encouraged to get a flu shot every fall. However, there have been no reported incidence of a reduction is symptomology, etiology or severity after the subjects receive the influenza vaccine. This phenomenon has not been observed, as a result from the administration of the immunogens or from the subjects' heightened immune response upon immunogen presentation.

According to Malecki et al. Polskie Archivum Medycyny Wewnetrznej. 2008; 18 (7-8): 435-440, there are many different types of diabetes, including MODY, mitochodtial diabetes, neonatal diabetes and lipoatrophic diabetes. These are in addition to diabetes types I and II, as well as gestational diabetes. See the abstract and the paragraph bridging pages 436-437. With so many types of diabetes, the skilled artisan would doubt that one treatment involving administering immunogens and/or meningicoccal immunogens would be effective in reducing the incidence or ameliroating the many forms of chronic diabetes.

Brydak et al. (Drugs. 2000; 60 (1): 35-53) review the immune responses in subjects with various chronic immune-mediated disorders, including the elderly, pulmonary diseases, diabetes mellitis, renal diseases, cancer, HIV infection and hemophilia. While a few of the immune responses in some subjects seemed depressed compared with others, overall protection was observed, see pages 37-49 and Tables 1-3. There were no observations indicating amelioration in symptomology, etiology or pathology for any of the subjects. The teachings of Brydak clearly indicate that not all chronic immune diseases are the same or that subjects with the disorders

respond the same way to immunogens. The skilled artisan would doubt that the administration of any immunogen would be ameliorative to any one or more chronic immune-mediated disorder.

Similarly, Rizaei et al. (Vaccine. 2008; 25: 5308-5314) discuss the protective success of administering polysaccharide meningococcal vaccines to children with primary antibody deficiencies (i.e. chronic immune-mediated disorders), see the abstract and Tables 1-3. While the majority of children responded favorably to the vaccine, there is no report or discussion of a reduction in severity of the chronic immune-mediated disorders in any of the children after vaccination.

More pertinent to the elected species of diabetes, Abdullah et al. (Vaccine (1998 Jan-Feb) Vol. 16, No. 2-3, pp. 156-60) discusses the encouragement of obtaining an influenza vaccine for diabetic subjects due to frequent complications if influenza is contracted. Abdullah et al. also compare the immune response in subjects with juvenile diabetes and healthy controls after administration of the vaccine. Abdullah et al. observes no difference in antibody response between different subjects. There is also no observation that the diabetic symptoms were ameliorated in the subjects with juvenile diabetes after receiving vaccination. See the abstract and Tables 1-3.

Gessner et al. (Pediatric Infectious Disease Journal. 2008. 27: 438-443) teaches that administration of the Hib vaccine and/or the DTP-hepatitis-Hib in infants 2-4 months old would prevent the incidence of pneumonia and meningitis, see the abstract and page 439. However, there is no recognition for reducing the incidence of the infants developing any chronic immune mediated disorder, or diabetes, as a result of receiving the vaccine(s).

Regarding pneumococcal vaccines against meningitis in high-risk children, including those with diabetes, Finn et al. (Arch. Dis. Child. 2002; 87:18-21) lists the high-risk groups on page 19. Finn concludes that further study is required to evaluate efficacy, safety, immunogenicity and optimal dosage regiments for the pneumococcal vaccines for children in high-risk groups, including those with diabetes. The lack of knowledge in the art is not bridged within the instant disclosure.

Snape et al. (JAMA. 2008; 299 (2): 173-184) teach the successful immunogenic response of a tetravalent meningococcal glycoconjugate vaccine in infants at 2, 3 and 4 or 2 and 4 months. There is no evidence that the vaccine will prevent or reduce the risk of developing a chronic immune disorder, or more specifically, diabetes, as a result of having received the vaccine.

The latest art that discusses the possibility of preventing the onset of diabetes through vaccination is Harrison (Immunology and Cell Biology. 2008; 86: 139-145). Harrison discussed this possibility through the administration of self-antigens. While this strategy has shown encouragement in rodent models, Harrison concedes that correlation in humans has failed. See the abstract and Table 1 on page 143. There is no discuss provided for reducing the risk of developing diabetes through administration of various immunogens, including those of meningococcal origin. There is no evidence that those with a predisposition for developing diabetes will avert development upon scheduled vaccination.

Zingg et al. Therapeutische unschau. Revue Therapeutique. 2005; 62 (10) 665-674, asks in the title of the article, "Does vaccination cause disease?" Zingg et al. concludes that the instant inventor's (JB Classen) suggested correlation between diabetes mellitus and Hib vaccinations are inconclusive due to the controversial data shown by DeStefano and Hviid, see

the Table bridging pages 671-672. In the summary section on page 674, Zingg et al. states: "**In large controlled trials there was no proof that… Hib-vaccination causes diabetes mellitus…**".

Similar conclusions are taught by, Levitsky. New England Journal of Medicine. 2004; 350 (14): 1380-1382. Levitsky specifically states on page 1382:

> Small studies have suggested possible relationships between the onset of diabetes and immunizations. However, these studies have not been supported by more rigorous epidemiologic examinations.4,5 In this issue of the *Journal,* Hviid and colleagues (pages 1398– 1404) report a retrospective review of a cohort of Danish children born between 1990 and 2000; they conclusively demonstrate that there is no relationship between vaccination history and the development of type 1 diabetes.

Indeed, the research of Hviid et al. New England Journal of Medicine. 2004; 350 (14): 1398-1404 reviewed the correlation between developing diabetes type 1 in 4,720,517 children that had received routine pediatric vaccinations between 1990 and 2000. Of the nearly 5 million children that were vaccinated during this time, only 681 children were diagnosed with diabetes type 1. Hviid et al. conclude that there is no nexus between childhood vaccination and the development of type 1 diabetes, see page 1398 and Table 2 on page 1402.

There is no discuss in the current state of the art for reducing the risk of developing or reducing severity of diabetes through administration of various immunogens, including those of meningococcal origin. There is no evidence that those with a predisposition for developing diabetes will avert development upon scheduled vaccination.

Such teachings are absent from the present disclosure. The disclosure teaches immunization of non-obese diabetic prone mice and diabetic prone BB rats as animal models for methods of treating diabetes in human (see Examples 1,2, and 3 beginning on pages 82, 83, and 85 respectively) and teaches that vaccination according to a specified schedule is preventative of the onset of diabetes in mice and rats. However, PIDJ (cited on page 9 of the non-final rejection mailed 6/20/2000) teaches that selective vaccines are protective against type 1 diabetes in mice, but not in humans, i.e., that the data generated from studies conducted using animal models is inconclusive in humans (see page 217, first column, third paragraph and page 218, the paragraph bridging columns 1 and 2). The disclosure also teaches analysis of retrospective immunization data as indicative of the efficacy of the claimed treatment methods (see pages 89-106). However, PIDJ teaches that "Ecologic studies may be used to generate hypotheses regarding possible factors associated with disease, but ecologic studies do not demonstrate causal relationships" (see page 219, the sentence bridging columns 1 and 2).

The disclosure contains the general teaching that the immunization protocols described for the diabetes animal models may also be used for mediating the onset and/or severity of other autoimmune diseases, see the paragraph bridging pages 21 and 22, for example. However, the disclosure is completely silent as to if and how the immunization protocols for the diabetes models are to be adapted for other autoimmune diseases. There are no working examples of any

animal models or epidemiological data regarding any autoimmune disease other than diabetes, and these experiments do not correlate with any predictability that any autoimmune disorder, including diabetes, would develop in response to a routine pediatric vaccination, as evidenced by the current state of the art.

The state of the art discussed herein shows a preponderance of conclusions regarding the invisible nexus between the development of chronic immune-mediated disorders, more particularly diabetes, and vaccinations. The inventor's own hypothesis between disease and vaccination were refuted in several references concerning the current state of the art for developing chronic immune-mediated disorders and vaccination. There is no evidence that would suggest to the skilled artisan that administration of any immunogen, or more specifically meningococcal immunogens, would reduce the incidence of developing a chronic immune-mediated disorder, such as diabetes, or that such an administration would reduce the severity of any chronic immune-mediated disease. The skilled artisan would not predict efficacy of the instant kits and methods using the instant kits, to ameliorate or prevent chronic immune-mediated diseases. There is no guidance provided or evidence in the instant working examples ameliorating the deficient veracity of the instant claims purporting a nexus between chronic immune-mediated disorders and immunization. An undue quantity of experimentation would be required of the skilled artisan to make and/or use the instant methods and intended use of the instant kits claimed.

Double Patenting

Claims 27, 59 and 102 are objected to under 37 CFR 1.75 as being substantial duplicate of claims. When two claims in an application are duplicates or else are so close in content that

they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). All three claims are drawn to a kit. Each kit of claims 27, 59 and 102 comprises the same physical components: …one or more containers, each container holding one or more pharmaceutically acceptable doses of one or more immunogens, said kit further comprising a label for each container…and instructions. "[F]ollowing such instructions" or "labeling indications", recited in the claims does not impart patentable distinctness on the components in the kit since printed matter is not functional, see MPEP § 2112.01 and *In re Gulack*, 703 F.2d 1381, 1385-86, 217 USPQ 401, 404 (Fed. Cir. 1983) ("Where the printed matter is not functionally related to the substrate, the printed matter will not distinguish the invention from the prior art in terms of patentability …. [T]he critical question is whether there exists any new and unobvious functional relationship between the printed matter and the substrate."). Since there is no functional relationship between the components in the kit and the paper the instructions are provided on, the printed material is indistinguishable between the claims. While the physical actions of "following such instructions" differ, there are no physical steps accomplished since the limitations of the kit comprise mere paper and immunogens in containers. Identical components in the kits of claims 27, 59 and 102 render the claims substantial duplicates.

Previous Double Patenting Issues

It is noted that there was a Double Patenting Rejection made against some of the instant claims and the claims of US 5,723,283 in the final rejection mailed November 5, 2001. Upon further consideration, it is determined that the instant claims and those of '283 are distinct. The claims of '283 are drawn to a method of determining whether an immunization schedule affects

the incidence or severity of a chronic immune-mediated disorder by administering immunogens to a treatment group and comparing its response with the response of an untreated control group. This method is distinct from the instant methods of reducing the incidence or severity of a chronic immune-mediated disorders and a method of protecting mammals from infectious diseases while reducing the risk of a chronic immune-mediated disease by administering immunogens.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 5, 6, 8, 10, 11, 16, 27-30, 32-41, 43, 44, 46, 49-52, 55-57, 59-62, 66-68, 71-74, 77, 84, 90-92, 96-112, 115-128 and 144-152 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 and 16-42 of U.S. Patent No. 5,728,385. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '385 anticipate the instant method claims. In

addition, the components required by the method claims of '385 would render the components of the instant kits obvious.

It is noted that the '385 patent is currently rendered invalid by the US District Court of Maryland, according to the decision submitted in the IDS of October 5, 2006. However, since the decision from the District Court is currently under appeal to the Federal Circuit Court, it has not been finally determined whether the '385 patent is invalid or not. Until a determination of invalidity is finally established, and/or Applicant successfully ameliorates the instant rejection, this rejection remains.

Claims 5, 6, 8, 10, 11, 16, 27-30, 32-41, 43, 44, 46, 49-52, 55-57, 59-62, 66-68, 71-74, 77, 84, 90-92, 96-112, 115-128 and 144-152 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-7, 10-13, 16, 17, 21, 26, 30, 31, 35, 38-41, 71, 73 and 77-108 of U.S. Patent No. 6,638,739. Although the conflicting claims are not identical, they are not patentably distinct from each other because although a comparison of immunization schedules is required in '739, the schedules claimed encompass the various regiments instantly claimed.

Claims 5, 6, 8, 10, 11, 16, 27-30, 32-41, 43, 44, 46, 49-52, 55-57, 59-62, 66-68, 71-74, 77, 84, 90-92, 96-112, 115-128 and 144-152 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-22, 26-41 and 63-70 of U.S. Patent No. 6,420,139. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of immunizing with the immunogens recited and the vaccination regiments anticipate the instant methods of immunizing. The

components used for immunization in the methods of '139 render the components of the instant kits obvious.

Claims 5, 6, 8, 10, 11, 16, 27-30, 32-41, 43, 44, 46, 49-52, 55-57, 59-62, 66-68, 71-74, 77, 84, 90-92, 96-112, 115-128 and 144-152 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10, 40-87, 97-106, 136-144, 170 and 196 of U.S. Patent No. 7,008,790. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of immunizing with the immunogens recited and the vaccination regiments anticipate the instant methods of immunizing. The components used for immunization in the methods of '790 render the components of the instant kits obvious.

Claims 5, 6, 8, 10, 11, 16, 27-30, 32-41, 43, 44, 46, 49-52, 55-57, 59-62, 66-68, 71-74, 77, 84, 90-92, 96-112, 115-128 and 144-152 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 7-22, 29, 58-82, 98-101, 110, 134, 150, 166-169, 175, 238, 240-246, 248 and 249 of copending Application No. 10/602,772. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of immunizing with the immunogens recited and the vaccination regiments anticipate the instant methods of immunizing. The components used for immunization in the methods of '790 render the components of the instant kits obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5, 8, 10, 11, 16, 27-30, 34-41, 43, 44, 46, 49-52, 55, 59-68, 71-74, 77, 84, 86-88, 90-92, 94-100, 102, 104-112, 115-128, 149-152, 259, 266-277 and 279-298 are rejected under 35 U.S.C. 102(b) as being anticipated by anticipated by Madore et al. (Pediatrics 85(3); 331-337, 1990).

Madore et al. teach immunizing l-month old infants (i.e., within the first 42 days of life) with a *Haemophilus influenza* type b oligosaccharide-CRM conjugate (i.e., a menigitis immunogen), see the abstract, the two paragraphs under "Vaccine" bridging pages 331-332 and Tables 1-5.

Claims 5, 8, 10, 11, 16, 27-30, 34-41, 43, 44, 46, 49-52, 55, 59-68, 71-74, 77, 84, 86-88, 90-92, 94-100, 102, 104-112, 115-128, 149-152, 259, 266-277 and 279-298 are rejected under 35 U.S.C. 102(b) as being anticipated by Dengrove et al. (Pediatric Research 20(8):745-739, 1986).

Dengrove et al. teaches DTP immunization in newborns and infants at 4 days of age in addition to the usual series at 2, 4, and 6 months of age (i.e., the first dose beginning before 42 days of age), see the abstract, "subjects, immunizations and specimens" section on page 735 and Figure 4.

Claims 5, 8, 10, 11, 16, 27-30, 34-41, 43, 44, 46, 49-52, 55, 59-68, 71-74, 77, 84, 86-88, 90-92, 94-100, 102, 104-112, 115-128, 149-152, 259, 266-277 and 279-303 are rejected under 35

U.S.C. 102(b) as being anticipated by Halsey et al. (Bulletin of the World Health Organization 63(6): 1151-1169, 1985).

Halsey et al. teaches immunization with a variety of vaccines within the 42 day window. Halsey et al. teaches vaccination with DPT at days 1-3, 5-8 (see Table 5) and at 4-8 weeks of age (page 1162, 2nd col.). Halsey et al. also teaches whole-cell pertussis vaccination at 1, 9, and 13 weeks demonstrated 64% protective efficacy (page 1162, 2nd col.). Halsey et al. further describes a study suggesting that improved protection against pertussis can be achieved by lowering the age of the first dose to one month (page 1162, 2nd col.). Halsey et al. also teaches the vaccination with a polio vaccine within the 42 day window (see Table 1).

Claims 5, 8, 10, 11, 16, 27-30, 34-41, 43, 44, 46, 49-52, 59-68, 71-74, 77, 84, 86-88, 90-92, 94-100, 102, 104-112, 115-128, 149-152 and 259 are rejected under 35 U.S.C. 102(b) as being anticipated by Jacob John (British Medical Journal 289: page 881 (1984).

John teaches the first dose of an oral poliomyelitis vaccine was given at day 7, 14, 21, 28, 35 or 42. John further suggests that the lower age limit for oral poliomyelitis vaccine should be 1 week and that the presence of maternal antibodies did not seem to inhibit the infant's ability to produce antibodies to the vaccine.

With regards to the kit claims, Applicant is reminded that though the claims include intended use limitations and/or other such functional language, intended use language is not given patentable weight. The physical components required within the instant kit are anticipated by the pharmaceutical formulations of Madore et al., Dengrove et al., Halsey et al., or John et al.

While the labeling of the immunogens taught by any of Madore et al., Dengrove et al., Halsey et al. or John et al. is not the same as that in the claimed kits, Applicant's printed matter is not given patentable weight over the kits and immunogens taught in the prior art, absent some functional relationship between the immunogens and the label or printed matter. "[F]ollowing such instructions" or "labeling indications", recited in the claims does not impart patentable distinctness on the components in the kit since printed matter is not functional, see MPEP § 2112.01 and *In re Gulack*, 703 F.2d 1381, 1385-86, 217 USPQ 401, 404 (Fed. Cir. 1983) ("Where the printed matter is not functionally related to the substrate, the printed matter will not distinguish the invention from the prior art in terms of patentability …. [T]he critical question is whether there exists any new and unobvious functional relationship between the printed matter and the substrate."). Since there is no functional relationship between the components in the kit and the paper the instructions are provided on, the printed material is indistinguishable between the instant claims and the prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHANON A. FOLEY whose telephone number is (571)272-0898. The examiner can normally be reached on M-F 5:30 AM-3 PM, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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